REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.9-11

Claims 4 and 5 are amended herein. New claims 17-20 are added herein. Basis for the amendments to the claims and new claims may be found throughout the specification and claims as-filed, especially at page 4, first and second paragraphs; and page 6, lines 7-9 and 9-11. Thus, no new matter is presented by way of the present Amendment.

The specification is amended herein to recite specific sequence identifiers for the six specific sequences listed in Example 1. However, Applicants note that in the Preliminary Amendment of November 7, 2002, sequence identifiers were added to the specification on behalf of the sequences referred to in the Brief Description of the Drawings as well as with regard to Example 1.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claim 4 stands rejected under 35 U.S.C. § 112, second paragraph, as purportedly failing to further limit base claim 1. Specifically, the recitation of "a foamy virus" where base claim 1 requires in the first DNA sequence at least part of a FeFV reverse transcript.

Claim 4, "a foamy virus" has been replaced with "the feline foamy virus", to clarify the claimed subject matter. Applicants submit this rejection is obviated.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claim 8 stands rejected under 35 U.S.C. § 112, first paragraph, as the specification is purportedly not enabling for a repeatable method for obtaining a full length FeFV clone. The Examiner notes that a biological deposit of the full length FeFV clone would satisfy the enablement requirement. To this end, Applicants submit herewith a copy of the deposit of pFeFV-7 (Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure—International Form) made with the DSMZ-Deutsche Sammlung Von Mikroorganismen und Zellkulturen GmbH depository, with the required Declaration. The Accession Number granted by the International Authority is DSM 12514. As noted in the Office Action, this deposit satisfies the enablement requirement on behalf of the FeFV clone.

Claims 1, 2, 4- 6, and 8-12 stand rejected under 35 U.S.C. § 112, first paragraph, because the specification, while enabling for a vector comprising a full length clone of FeFV, is purportedly not enabling for vectors containing only a portion of the genome. Applicants traverse, and state that the specification provides sufficient guidance to permit the skilled artisan to make and use the full scope of the claimed invention.

The specification discloses a full-length viral DNA vector, which is suitable as a source for modified vectors having reduced viral DNA vector which is suitable as a source for modified vectors having reduced viral elements. For example, page 5 of the specification discloses that the full-length DNA sequence may be modified regarding its length or various nucleotide additions, deletions or substitutions. Such methods are well known in the art. Further, the specification describes self-

replicating, replication-competent as well as replication-defective vectors as examples for genetically modified vector types (*see* the paragraph bridging pages 3 and 4). Regarding replication-competent vectors, the specification indicates that the regulatory "bel" genes are required for the replication of the virus (*see* page 2, 2nd paragraph) and suggests to inactivate the Bel 1 transactivator (*see* page 4, 2nd paragraph).

Regarding replication-defective vectors, the specification provides instructions for replacing structural genes by the foreign DNA (*see* page 4, 1st paragraph). These instructions in the specification are in accordance with the state of the art at the time the present application was filed.

Applicants enclose herewith an excerpt of chapter 9 of the book "Retroviruses" (edited by John M. Coffin, Stephen H. Hughes and Harold E. Varmus (1997)) as evidence of the state of the art relating to the design of retroviral vectors. On page 438, right hand column, it discloses retroviral elements which are critical for gene transduction and integration. Further, page 437 discloses that it has been well known from studies dating back to 1981 that retroviral genomes can accommodate extensive alterations and deletions. Ventors based on human FV to deliver heterologous genes have been reported in the prior art (*e.g.*, Schmidt *et al.*).

In light of the above, the skilled artisan could readily couple the disclosure of the full-length-clone and the two described vector types in the specification with the known methods for constructing retroviruses to derive modified vectors which comprise less than the full-length FeFV clone. The experimentation needed to practice the full-scope of the invention is not undue, because all methods needed to practice the invention are well known. In fact, the specification provides a method to

easily determine by means of common methods whether the derived part of the DNA sequence still meets the necessary conditions of a retroviral vector, *i.e.*, transfection of the recombinant FeFV DNA in permissive CRFK cells. It would not require undue experimentation to obtain vectors comprising at least part of a FeFV, due to the sufficient amount of information about the design of retroviruses comprising reduced viral elements well known in the art.

Rejections Under 35 U.S.C. § 103

Claims 1- 12 stand rejected under 35 U.S.C. § 103(a) as purportedly unpatentable over Winkler *et al.* (*Journal of Virology* 1997, Vol. 71, pages 6727-6741) and Schmidt *et al.* (*Virology* 1995, Vol. 210, pages 167- 178). The Office Action states that Winkler *et al.* disclose the same clone as used in the invention and that the clone may be used to make vectors for targeted gene delivery. However, Winkler fails to disclose the making of a retroviral vector.

In order to establish a case of *prima facie* obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation to modify the reference or combine reference teachings, (2) there must be a reasonable expectation of success, and (3) the prior art reference(s) must teach or suggest all of the claim limitations. *See* M.P.E.P. 2142. Applicants respectfully submit that these criteria have not been met in the present Office Action.

The cited references, alone or in combination, fail to recite all of the elements of the presently claimed invention or to provide an expectation of success or motivation to arrive at the claimed invention.

The presently claimed invention is directed to a retroviral vector for introducing an expressible DNA into a mammalian cell. The retroviral vector comprises a first DNA sequence corresponding to the reverse transcript of at least part of a feline foamy virus (FeFV), and a second DNA sequence permitting the propagation in bacteria.

Winkler *et al.* do not teach the same clone, the FeFV clone, as used in the invention. Nor does Winkler *et al.* disclose that it can be used to make vectors. Winkler *et al.* merely disclose the complete genomic sequence and genomic organization of the FeFV. None of the clones disclosed by Winkler *et al.* comprise the full-length DNA of FeFV. The only mention of FeFV in on page 6740 of Winkler *et al.*, where it is merely mentioned that "it will be interesting to examine FeFV as a retroviral vector". This disclosure does not indicate or suggest that the disclosed subgenomic FeFV DNA clones would be suitable to make retroviral vectors.

Furthermore, the engineering of a FeFV vector is not possible by simply using the data and information provided by Winkler *et al.* In order to generate new viral vectors, it is absolutely essential to first construct an infectious, fully replication-competent DNA genome of the virus. None of the sub-genomic DNA fragments described in Winkler *et al.* are infectious. Nor does Winkler *et al.* provide a full-length FeFV DNA clone. On page 6728, right column, lines 5 and 6 from the bottom, it is noted that "repeated attempts to clone this (*i.e.* full length) DNA into different vectors did not result in any stable recombinant clone". Thus, a skilled person would not have a reasonable expectation of success from the teaching of Winkler *et al.*, because a full length viral DNA clone is necessary for generating novel viral vectors. Winkler *et al.* do not indicate how a full length clone could be obtained. Winkler *et al.*

disclose only sub-genomic clones which are not infectious and cannot form a basis for the development of viral vectors.

Schmidt *et al.* fails to overcome the deficiencies of Winkler *et al.* Schmidt *et al.* disclose human FV vectors. However, Schmidt *et al.* also disclose that the source of all vectors was the full length viral DNA clone (page 168, left column, 1st paragraph and Fig. 1A). Thus, the teaching of Schmidt *et al.* confirms, as discussed above, that a full length, infectious DNA genome of the virus has to be constructed to generate novel viral vectors.

Winkler *et al.* did not succeed in providing a full length FeFV DNA clone and Schmidt *et al.* do not indicate how such a full length FeFV DNA clone may be obtained. Thus, the combination of both teachings would not lead a skilled person to the present invention or provide the skilled artisan with an expectation of success.

In fact, it is unexpected that the present invention, using different and additional procedures, was able to successfully engineer the full length pFeFV-7 DNA clone disclosed (*see* page 11 of the specification). It was not possible to make a full length proviral clone by simply ligating the partial clones of Winkler *et al.* None of the methodological steps described on page 11 of the specification which were necessary to obtain the full length FeFv clone and from which FeFV vector derivatives comprising a part of a FeFV can be constructed are indicated in the cited reference.

Winkler *et al.* and Schmidt *et al.*, taken in combination, fail to provide any expectation of success, and to teach or suggest all of the elements of the claims. Thus, Applicants request that the rejection under 35 U.S.C. § 103 be withdrawn.

CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: November 3, 2004

By: _____
Deborah H. Yellin
Registration No. 45,904

P.O. Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

VA 393005.1